UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,392	08/21/2002	Kotoku Kurachi	UM-06855	7886

7590 10/20/2005

Medlen & Carroll
Suite 350
101 Howard Street
San Francisco, CA 94105

EXAMINER	
NGUYEN, QUANG	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 10/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,392	KURACHI ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *3-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Attached sequence searches*.

DETAILED ACTION

Claims 1-20 are pending in the present application.

Applicant's election without traverse of Group II (claims 1-2) in the reply filed on 8/18/05 is acknowledged.

Claims 3-20 are withdrawn from further consideration because they are drawn to non-elected inventions.

Claims 1-2 are examined on the merits herein.

Priority

If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 120, a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. **For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.**

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the

application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge

under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

Applicant's invention is drawn to a recombinant expression vector comprising in operable combination i) a nucleic acid sequence of interest, ii) a promoter sequence and iii) one or more age regulatory sequences selected from SEQ ID NO:3 and any

portion of SEQ ID NO:3; and a method for expressing a nucleic acid sequence of interest in a cell containing the same expression construct.

Apart from disclosing that the entire SEQ ID NO:3 (AE') and at best the 102-nucleotide nucleic acid stem-loop forming sequence of SEQ ID NO:91 (AE") within SEQ ID NO:3 confer an age-associated stable gene expression pattern, the instant specification fails to describe any other essential core structural elements within the SEQ ID NO: 3 that have an age regulatory activity. The instant specification fails to disclose a representative number of species of a broad genus of a portion of SEQ ID NO:3 having an age-regulatory activity. At about the filing date of this application (6/6/200), Applicants still state "[w]e have identified another unique structure in the 3' UTR, AE3', which is responsible for the 3' UTR's critical function in age regulation of hFIX gene. This function of AE3' presumably is due to the sl structure-forming dinucleotide repeats that are present in the 3' UTR" (page 743, first column, first paragraph; Science 285:739-743, 1999). Additionally, even in 2002 the underlying mechanism for the induction of age-associated elevation of mRNA levels mediated by these two age-related increase elements remain to be elucidated (Zhang et al., J. Biol. Chem. 277:4532-4540, 2002; page 4538, second column, second full paragraph).

The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants' filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant

identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a representative number of species for a broad genus of a recombinant expression vector containing any portion of SEQ ID NO:3 as an age regulatory sequence, and a method for expressing a nucleic acid sequence of interest in a cell using the same. Therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

1. A recombinant expression vector comprising in operable combination i) a nucleic acid sequence of interest, ii) a promoter sequence and iii) one or more age regulatory sequences selected from SEQ ID NO:3 and a nucleic acid sequence

comprising SEQ ID NO: 91, wherein the age regulatory sequences are located 3' of said nucleic acid sequence of interest;

2. A method of expressing a nucleic acid sequence of interest in an isolated cell, comprising:

a) providing: i) an isolated cell, ii) a nucleic acid sequence of interest, iii) a promoter sequence, and iv) one or more age regulatory sequences selected from SEQ ID NO:3 and a nucleic acid sequence comprising SEQ ID NO: 91,

b) operably linking said nucleic acid sequence of interest, said promoter sequence and said one or more age regulatory sequences, wherein the age regulatory sequences are located 3' of said nucleic acid sequence of interest to produce a transgene; and

c) introducing said transgene into said isolated cell to create a treated cell under conditions such that said nucleic acid sequence of interest is expressed in said treated cell;

does not reasonably provide enablement for other recombinant expression vector containing any other portions of SEQ ID NO:3 as an age-regulatory sequence or in any other operable combinations or a method of introducing a transgene into a cell *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in the determination of an enabling disclosure have been summarized as the quantity of experimentation necessary, the amount of direction

or guidance presented, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex parte Forman*, (230 USPQ 546 (Bd Pat. Appl & Unt, 1986); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)).

The present specification is not enabled for the instant broadly claimed invention for the reasons discussed below.

(a) The breadth of the claims

The claims encompass a recombinant expression vector comprising in any operable combination i) any nucleic acid sequence of interest, ii) any promoter sequence and iii) one or more age regulatory sequences selected from SEQ ID NO:3 and any portion of SEQ ID NO:3 (e.g., including any fragment from 5 contiguous nucleotide residues of SEQ ID NO:3, see specification page 31, lines 8-11); and a method for expressing any nucleic acid sequence of interest in any cell (both *in vitro* and *in vivo*) by introducing into the cell the same expression construct or a transgene.

When read in light of the specification, an embodiment of the method of claim 2 encompasses a gene therapy method by introducing into any cell *in vivo* the expression construct of the present invention (at least page 61-65). Please note that enablement requires the specification to teach how to make and/or use the claimed invention.

(b) The state and the unpredictability of the art

At about the filing date of the present application (6/6/2000), little was known about any age-related regulatory activity of SEQ ID NO:3, let alone for any portion thereof as evidenced by the teachings of Kurachi et al. (Science 285:739-743, 1999);

Kurachi et al. (Arteroscler. Thromb. Vasc. Biol. 20:902-906, 2000) and Zhang et al. (J. Biol. Chem. 277:4532-4540, 2002). Kurachi et al. (Science 285:739-743, 1999) state "[w]e have identified another unique structure in the 3' UTR, AE3', which is responsible for the 3' UTR's critical function in age regulation of hFIX gene. This function of AE3' presumably is due to the sl structure-forming dinucleotide repeats that are present in the 3' UTR" (page 743, first column, first paragraph). Even in 2002, Zhang et al still state "the age-related increase of circulatory hPC in the animals carrying –1462hPCm1/AIE was accompanied by a similar age-related increase pattern in the liver mRNA level (Fig. 6G), suggesting that AIE function to induce age-associated elevation of mRNA levels, most likely through increasing mRNA stability. The underlying molecular mechanisms remain to be elucidated." (page 4538, second column, second full paragraph).

Additionally, with respect to an embodiment of claim 2, the state of the gene therapy art was and still remains unpredictable with respect to the attainment of any desired therapeutic effect as evidenced by the reviews of Dang et al. (Clin. Cancer Res. 5:471-474, 1999), Romano et al. (Stem Cells 18:19-39, 2000) and Verma et al. (Annu. Revi. Biochem. 74:711-738, 2005). Dang et al. stated "Although significant progress has been achieved in our understanding of the limitations of gene therapy by suboptimal vectors, host immunological responses to the vectors, and the lack of long term stable expression, the major challenge that limits clinical translation remains in achieving efficient gene delivery to target tissues" (page 474, col. 2, last paragraph). Romano et al. stated "The potential therapeutic applications of gene transfer technology are enormous. However, the effectiveness of gene therapy programs is still questioned"

(see abstract), and "Despite the latest progress reported in the area of vector design, research strategies still have to tackle critically important issues, such as further improvement of gene transfer technology, especially for *in vivo* gene delivery applications, regulation and control of the transgene expression post-cell transduction, and a variety of complex safety matters. Even in 2005, Verma et al. (Annu. Revi. Biochem. 74:711-738, 2005) still state "The young field of gene therapy promises major medical progress toward the cure of a broad spectrum of human diseases, ranging from immunological disorders to heart disease and cancer. It has, therefore, generated great hopes and great hypes, but it has yet to deliver its promised potential", and "[I]f scientists from many different disciplines participate and pull together as a tem to tackle the obstacles, gene therapy will be added to our medicinal armada and the ever-expanding arsenal of new therapeutic modalities." (page 732, top of third paragraph).

Thus, it is clear that at the filing date of the present application gene therapy for any treatment was and continues to be immature and unpredictable.

(c) The amount of direction or guidance presented

Apart from the exemplification showing that the entire SEQ ID NO:3 (AE') and at best the 102-nucleotide nucleic acid stem-loop forming sequence of SEQ ID NO:91 (AE") within SEQ ID NO:3 are capable of conferring an age-associated stable gene expression pattern, the instant specification fails to provide sufficient guidance for a skilled artisan on how to make and/or use any other age-regulatory sequence fragments of SEQ ID NO:3 that do not comprise at least the AE" element. The instant specification also does not provide sufficient guidance for a skilled artisan on how to

make and use any of the instant invention's age-regulatory sequence in any operable combination other than the age-regulatory sequence has to be 3' of the nucleic acid sequence of interest. Zhang et al. clearly demonstrated that AE" does not function as a transcriptional enhancer to confer its age-associated stable gene expression pattern (page 4538, second column, second full paragraph). The instant specification further fails to provide any evidence indicating or suggesting that any therapeutic effect has been attained *in vivo* through the use of any of Applicant's recombinant expression vectors, particularly in light of the state and the unpredictability of obtaining any therapeutic effect via gene therapy as discussed above. Thus, given the lack of sufficient guidance provided by the present application, it would have required undue experimentation for a skilled artisan to make and use the recombinant expression vector and the method as claimed.

As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> That scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the are; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

Accordingly, due to the lack of sufficient guidance provided by the specification regarding to the issues discussed above, the unpredictability of the gene therapy, and the breadth of the instant claims, it would have required undue experimentation for one skilled in the art to make and use the instant broadly claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 2, due to the lack of a preamble and the opening language of the term "comprising", it is unclear exactly which method that Applicants intend to claim. The metes and bounds of the claim are not clearly determined. Clarification is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2 are rejected under 35 U.S.C. 102(a) as being anticipated by Kurachi et al. (J. Biol. Chem. 270:5276-5281, 1995) as evidenced by Yoshitake et al. (Biochemistry 24:3736-3750, 1985).

Kurachi et al disclose the construction of a set of three human factor IX minigene expression vectors, p-416FIXc, p-416FIXm1 and p-416FIXm2, and the p-416FIXm1 and p-416FIXm2 constructs containing a truncated intron 1 of the factor IX gene showed 7-9 fold higher expression activities than p-416FIXc that does not contain a factor IX intron 1 sequence (see abstract). All of the expression vector constructs contain the human factor IX exon VIII along with 3' flanking genomic sequences (Figure 2). The human factor IX exon VIII (nucleotides 30822-32757) comprises the 3' UTR having SEQ ID NO:3 (nucleotides 31,418-32,690) as evidenced by the disclosure of Yoshitake et al. (see Figure 3, Table I and the attached sequence search). Accordingly, all the expression vector constructs of Kurachi et al. contain the 3' UTR having SEQ ID NO:3.

Kurachi et al further teach the transfection of HepG2 cells with the aforementioned human factor IX minigene expression vectors (page 5277, right-hand col., fourth paragraph), and the expression of factor IX in the cell cultures was assayed (Table II and Fig. 4).

Accordingly, the teachings of Kurachi et al meet all limitation of the claims as written, and therefore the reference anticipates the instant claims.

Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Clark, A.J (WO 95/3000).

Clark teaches an improved and modified factor IX expression construct FIX-Δ3' splice containing an encoded truncated 3' UTR that falls within the scope of a portion of the 3'-UTR having SEQ ID NO:3 (see Fig. 2 and the attached sequence search) and an

expression control sequence such as a promoter for expression in a suitable host cell (at least page 5, line 8 continues to line 16 of page 6 and particularly example 4).

The teachings of Clark meet all limitation of the claims as written, and therefore the reference anticipates the instant claims.

Claims 1-2 are rejected under 35 U.S.C. 102(e) as being anticipated by Stafford et al. (US 6,531,298).

Stafford et al teach an expression cassette containing a nucleic acid encoding a mammalian factor IX protein, including the nucleic acid of SEQ ID NO:1 that contains a 3' UTR that is 99.8% sequence similarity to SEQ ID NO:3 (see SEQ ID NO:1). Stafford et al further teach that the nucleic acid sequence is operably linked to suitable control sequences (e.g., a promoter) in a replicable DNA or RNA construct such as plasmids, adenovirus, adenoassociated virus, retroviruses and others for expression in a host cell (col. 4, line 19 continues to line 5 of col. 5).

Accordingly, the teachings of Stafford et al meet all limitation of the claims as written, and therefore the reference anticipates the instant claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of copending Application No. 11/129861.

Although the conflicting claims are not identical, they are not patentably distinct from each other because a recombinant expression vector comprising in operable combination i) a nucleic acid sequence of interest, ii) a promoter sequence, and iii) one or more age regulatory sequences selected from the group consisting of SEQ ID NO:3 and a functional portion of SEQ ID NO:3, and a method of expressing a nucleic acid sequence of interest in a mammalian cell and a method of expressing factor IX in a mammalian cell in the co-pending Application No. 11/129861 anticipate the claimed genus in the application being examined and, therefore, a patent to the genus would, necessarily, extend the rights of the species or sub- should the genus issue as a patent after the species of sub-genus.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

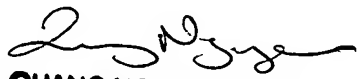
If attempts to reach the examiner by telephone are unsuccessful, the examiner's primary Celine Qian, Ph.D., may be reached at (571) 272-0777, or SPE, Dave Nguyen, at (571) 272-0731.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



QUANG NGUYEN, PH.D
PATENT EXAMINER